

The listing of claims will replace all prior versions, and listings, of claims in the application. Please cancel claims 1-16 and 57-62 without prejudice. Please amend claims 17, 23, 24, 29, 30, 31, 37, 40, 41, 43, and 48 as follows.

Listing of Claims:

Claims 1-16 (Cancelled).

Claim 17 (Currently Amended): A composition comprising a prodrug, the prodrug comprising

a therapeutically active drug; and

a peptide ~~of claim 1~~ comprising an amino acid sequence having a cleavage site specific for an enzyme having a proteolytic activity of human kallikrein 2 (hK2), wherein the peptide is 20 or fewer amino acids in length,

wherein the peptide is linked to the therapeutically active drug to inhibit the therapeutic activity of the drug, and wherein the therapeutically active drug is cleaved from the peptide upon proteolysis by an enzyme having a proteolytic activity of human kallikrein 2 (hK2).

Claim 18 (Original): The composition of claim 17, wherein the peptide is linked directly to the therapeutic drug.

Claim 19 (Original): The composition of claim 18, wherein the peptide is linked directly to a primary amine group on the drug.

Claim 20 (Original): The composition of claim 17, wherein the peptide is linked to the therapeutic drug via a linker.

Claim 21 (Original): The composition of claim 20, wherein the linker is an amino acid sequence.

Claim 22 (Original): The composition of claim 21, wherein the linker comprises a leucine residue.

Claim 23 (Currently Amended): The composition of claim 17, wherein the therapeutically active drug inhibits a sarcoplasmic reticulum and endoplasmic reticulum Ca^{2+} -ATPase (SERCA) pump.

Claim 24 (Currently Amended): The composition of claim 23, wherein the therapeutically active drug is selected from the group of primary amine containing thapsigargins ~~or~~ and thapsigargin derivatives.

Claim 25 (Original): The composition of claim 17, wherein the therapeutically active drug intercalates into a polynucleotide.

Claim 26 (Original): The composition of claim 25, wherein the therapeutically active drug is an anthracycline antibiotic.

Claim 27 (Original): The composition of claim 26, wherein the therapeutically active drug is selected from the group consisting of doxorubicin, daunorubicin, epirubicin and idarubicin.

Claim 28 (Previously Amended) The composition of claim 17, wherein the peptide is Gly-Gly-Lys-Ala-Arg-Arg-Leu (SEQ ID NO:135).

Claim 29 (Currently Amended): The composition of claim ~~17~~ 20, wherein the therapeutic drug is a compound belonging to the group of thapsigargins which have been derivatized with a moiety containing a primary amine group, the peptide is Gly-Gly-Lys-Ala-Arg-Arg-Leu (SEQ

ID NO:135), and the linker is selected from the group consisting of: ~~unsubstituted or alkyl-, aryl-, halo-, alkoxy-, alkenyl-, amido- or amino-substituted~~

- (a) $\text{CO}-(\text{CH}=\text{CH})_{n1}-(\text{CH}_2)_{n2}-\text{Ar}-\text{NH}_2$,
- (b) $\text{CO}-(\text{CH}_2)_{n2}-(\text{CH}=\text{CH})_{n1}-\text{Ar}-\text{NH}_2$,
- (c) $\text{CO}-(\text{CH}_2)_{n2}-(\text{CH}=\text{CH})_{n1}-\text{CO}-\text{NH}-\text{Ar}-\text{NH}_2$,
- (d) $\text{CO}-(\text{CH}=\text{CH})_{n1}-(\text{CH}_2)_{n2}-\text{CO}-\text{NH}-\text{Ar}-\text{NH}_2$,
- (e) $\text{CO}-(\text{CH}_2)_{n3}-\text{NH}_2$, and
- (f) $\text{CO}-(\text{CH}_2)_{n3}-\text{NH}-\text{CO}-\text{CH}(\text{R}_4)-\text{NH}_2$,

each of which is unsubstituted or alkyl-, aryl-, halo-, alkoxy-, alkenyl-, amido- or amino-substituted, and wherein $n1$ and $n2$ are from 0 to 5, $n3$ is from 0 to 15, Ar is any substituted or unsubstituted aryl group, attachment of NH_2 to Ar is in a ortho, meta or para position with respect to the remainder of the linker, and R_4 is any naturally occurring amino acid side chain.

Claim 30 (Currently Amended): The composition of claim 17, wherein the therapeutically active drug has an IC_{50} LC_{50} toward ER Ca^{2+} -ATPase of at most 500 nM.

Claim 31 (Currently Amended): The composition of claim 30, wherein the therapeutically active drug has an IC_{50} LC_{50} toward ER Ca^{2+} -ATPase of at most 50 nM.

Claim 32 (Original): The composition of claim 17, wherein the therapeutically active drug has an LC_{50} toward hK2-producing tissue of at most 20 μM .

Claim 33 (Original): The composition of claim 32, wherein the therapeutically active drug has an LC_{50} toward hK2-producing tissue of less than or equal to 2.0 μM .

Claim 34 (Original): The composition of claim 17, further comprising an added substituent which renders the composition water soluble.

Claim 35 (Original): The composition of claim 34, wherein the added substituent is a polysaccharide.

Claim 36 (Original): The composition of claim 35, wherein the polysaccharide is selected from the group consisting of modified or unmodified dextran, cyclodextrin and starch.

Claim 37 (Currently Amended): A method of producing a prodrug, the method comprising the step of linking

a therapeutically active drug and

a peptide ~~of claim 1~~ comprising an amino acid sequence having a cleavage site specific for an enzyme having a proteolytic activity of human kallikrein 2 (hK2), wherein the peptide is 20 or fewer amino acids in length,

wherein the linking of the peptide to the drug inhibits the therapeutic activity of the drug.

Claim 38. (Original): The method of claim 37, wherein the therapeutically active drug has a primary amine.

Claim 39 (Original): The method of claim 37, wherein the prodrug contains a linker between the peptide and the drug.

Claim 40 (Currently Amended): The method of claim 39, wherein the linker is an amino acid sequence which comprises ~~Leu~~ leucine.

Claim 41 (Currently Amended): The method of claim 37, wherein the peptide further comprises a capping group attached to the N-terminus of the peptide, the capping group inhibiting endopeptidase activity on the peptide.

Claim 42 (Original): The method of claim 41, wherein the capping group is selected from the group consisting of acetyl, morpholinocarbonyl, benzyloxycarbonyl, glutaryl, and succinyl substituents.

Claim 43 (Currently Amended): A method of treating a ~~hK2-producing~~ cell proliferative disorder which produces hK2, the method comprising administering the composition of claim 17 in a therapeutically effective amount to a subject having the cell proliferative disorder.

Claim 44 (Original): The method of claim 43, wherein the disorder is benign.

Claim 45 (Original): The method of claim 43, wherein the disorder is malignant.

Claim 46 (Original): The method of claim 45, wherein the malignant disorder is prostate cancer.

Claim 47 (Original): The method of claim 45, wherein the malignant disorder is breast cancer.

Claim 48 (Currently Amended): A method of detecting human kallikrein 2-producing tissue, the method comprising:

contacting the tissue with a composition comprising

a detectably labeled peptide ~~of claim 1~~ for a period of time sufficient to allow cleavage of the peptide, where the peptide comprises an amino acid sequence having a cleavage site specific for an enzyme having a proteolytic activity of human kallikrein 2 (hK2), wherein the peptide is 20 or fewer amino acids in length, and wherein the peptide comprises a detectable label; and

detecting the detectable label.

Claim 49 (Original): The method of claim 48, wherein the peptide further comprises a capping group attached to the N-terminus of the peptide, the group inhibiting endopeptidase activity.

Claim 50 (Original): The method of claim 49, wherein the capping group is selected from the group consisting of acetyl, morpholinocarbonyl, benzyloxycarbonyl, glutaryl, and succinyl substituents.

Claim 51 (Original): The method of claim 48, wherein the detectable label is a fluorescent label.

Claim 52 (Original): The method of claim 51, wherein the fluorescent label is selected from the group consisting of 7-amino-4-methyl coumarin, 7-amino-4-trifluoromethyl coumarin, rhodamine 110, and 6-aminoquinoline.

Claim 53 (Original): The method of claim 48, wherein the detectable label is a radioactive label.

Claim 54 (Original): The method of claim 53, wherein the radioactive label is selected from the group consisting of tritium, carbon-14, and iodine-125.

Claim 55 (Original): The method of claim 48, wherein the detectable label is a chromophoric label.

Claim 56 (Original): The method of claim 48, wherein the detectable label is a chemiluminescent label.

Claims 57-62 (Cancelled).